PATENT USSN 09/942,087 Docket No. 8325-0002.21 Ref. No. S2-US5

AMENDMENTS TO THE CLAIMS

This listing of claims replaces all prior listings and versions.

1. (previously presented) A method of modulating expression of an endogenous cellular gene in a cell, the method comprising the step of:

contacting the cell with a first polynucleotide encoding a first zinc finger protein, wherein the first zinc finger protein is a fusion protein comprising a designed or selected zinc finger protein in operative linkage with a functional domain, further wherein the fusion protein binds to a first target site in the gene;

thereby modulating expression of the endogenous cellular gene.

- 2. (previously presented) The method of claim 1, wherein the step of contacting further comprises contacting the cell with a second polynucleotide encoding a second zinc finger protein that binds a second target site in the endogenous cellular gene.
- 3. (original) The method of claim 2, wherein the first and second target sites are adjacent.
- 4. (original) The method of claim 3, wherein the first and second zinc finger proteins are covalently linked.
- 5. (original) The method of claim 1, wherein the first zinc finger protein is a fusion protein comprising at least two regulatory domains.
- 6. (original) The method of claim 3, wherein the first and second zinc finger proteins are fusion proteins, each comprising a functional domain.
- 7. (previously presented) The method of claim 6, wherein the first and second zinc finger proteins are fusion proteins, each comprising at least two functional domains.

- 8. (previously presented) The method of claim 1, wherein the cell is selected from the group consisting of an animal cell, a plant cell, a bacterial cell, a protozoal cell, or a fungal cell.
 - 9. (original) The method of claim 8 wherein the cell is a plant cell.
 - 10. (original) The method of claim 8, wherein the cell is a mammalian cell.
 - 11. (original) The method of claim 10, wherein the cell is a human cell.
- 12. (original) The method of claim 1 wherein the expression of the endogenous cellular gene is repressed.
- 13. (currently amended) The method of claim 12, wherein the functional domain is selected from the group consisting of unliganded thyroid hormone receptor (TR), verbA, Dax[[,]] and RBP, MeCP2, MBD2B and a DNMT.
- 14. (original) The method of claim 1, wherein the expression of the endogenous cellular gene is activated.
- 15. (original) The method of claim 14, wherein the functional domain is ligand-bound thyroid hormone receptor.
- 16. (original) The method of claim 15, wherein the ligand is 3,5,3'-triiodo-L-thyronine (T3).
- 17. (original) The method of claim 1 wherein the functional domain is a bifunctional domain (BFD).

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- 18. (original) The method of claim 17, wherein the activity of the bifunctional domain is dependent upon interaction of the BFD with a second molecule.
- 19. (original) The method of claim 18, wherein the BFD is selected from the group consisting of thyroid hormone receptor, retinoic acid receptor, estrogen receptor and glucocorticoid receptor.
 - 20. (original) The method of claim 18, wherein the second molecule is a protein.
- 21. (original) The method of claim 18, wherein the second molecule is a small molecule.
- 22. (original) The method of claim 19, wherein the second molecule is a small molecule.
- 23. (original) The method of claim 22, wherein the small molecule is selected from the group consisting of thyroid hormone (T3), all-*trans* retinoic acid, estradiol, tamoxifen, 4-hydroxy-tamoxifen, RU-486 and dexamethasone.

24. (canceled)

- 25. (previously presented) The method of claim 1, wherein sequences encoding the first zinc finger protein are operably linked to a promoter, and wherein the first polynucleotide is administered to the cell in a lipid:nucleic acid complex or as naked nucleic acid.
- 26. (previously presented) The method of claim 1, wherein sequences encoding the first zinc finger protein are contained in an expression vector and are operably linked to a promoter, and wherein the method further comprises the step of first administering the expression vector to the cell.

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- 27. (original) The method of claim 26, wherein the expression vector is a viral expression vector.
- 28. (original) The method of claim 27, wherein the expression vector is selected from the group consisting of a retroviral expression vector, an adenoviral expression vector, and an AAV expression vector.
- 29. (previously presented) The method of claim 25, wherein the promoter is an inducible promoter.
- 30. (previously presented) The method of claim 26, wherein the promoter is an inducible promoter.
- 31. (previously presented) The method of claim 1, wherein the first target site is upstream of a transcription initiation site of the endogenous cellular gene.
- 32. (previously presented) The method of claim 1, wherein the first target site is adjacent to a transcription initiation site of the endogenous cellular gene.
- 33. (previously presented) The method of claim 1, wherein the first target site is downstream of a transcription initiation site of the endogenous cellular gene.
- 34. (original) The method of claim 1, wherein the zinc finger protein comprises an SP-1 backbone.